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Metabolomic study of patients with bipolar disorder through ¹H Nuclear Magnetic Resonance (NMR)

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Abstract

The Bipolar Disorder (BD) is a psychiatric illness that affects 1% of the global population. Having in mind that diagnostics of the BD is difficult and based only on clinical evaluation, our current research has as objective the comparison of the metabolic profiles between Healthy Control (HC) group and the BD patients. Also, we aim to find the substantial differences that can suggest biomarkers for BD and, finally, to connect them with pathophysiological conditions of this disorder. To enlarge results obtained in previous studies of BD biomarkers (done with limited number of BD patients), the blood serum samples were analyzed using ¹H Nuclear Resonance Magnetic (NMR) spectroscopy and chemometric methods in the data analysis. As result, the most important regions in the ¹H NMR spectra responsible for samples classification into two groups have been identified to be from 1.0 to 4.0 ppm and confirmed our previous results. Until now we have analysed 22 serum samples from the BD patients and 26 samples of HC Group. The expectation is to analise 100 samples, 50 of each group. Our partial results point 18 metabolites as possible biomarkers for the BD, among which myo-inositol, coline, valine, lactate, creatine, threonine, L-aspartate and GABA are the most important.

Key words:

Bipolar Disorder, Metabolomics and Biomarkers.

Introduction

The BD is a psychiatric illness that affects 1% of the global population[1] and it has been one of the ten biggest incapacitating disorders that affect adults during their productive age. In addition, elevated rates of relapse during treatment are commonly associated with errors in diagnosis[2, 3], which is done only by interview with the patients, their familiars and close friends. The absence of cure and limitations of available treatments to bipolar disorder reflect the limited knowledge that we have of brain and its cellular and molecular mechanisms. To try to add new insights in BD, metabolomics studies were done and they have revealed some differences between metabolic profiles of patients with BD and individuals from the HC group, mainly provoked by lipids[4]. However, these studies were done with a small number of samples. Thereby, current research has as objective the comparison of the metabolic profiles between HC and BD groups aiming to find substantial differences among them. These can lead to identification of biomarkers for BD that could be linked with pathophysiological conditions of this disorder. Thus, the blood serum samples of patients with BD were analyzed using ¹H Nuclear Resonance Magnetic (NMR) spectroscopy and chemometrics tools in the data analysis, such as Principal Component Analysis (PCA) and Partial least squares Discriminant Analysis (PLS-DA).

Results and Discussion

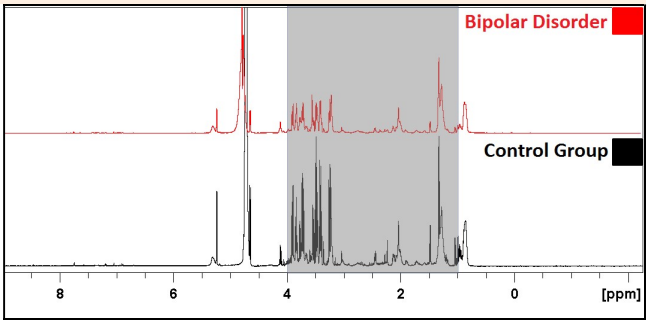

Figure 1: NMR spectra obtained with a T_2 filter of blood serum samples from the patient with BD **(red)** and an individual from HC group **(black)**. The two NMR spectra are shown in the same intensity scales and the shaded area indicates the region used in chemometrics (1.00 to 4.00 ppm).

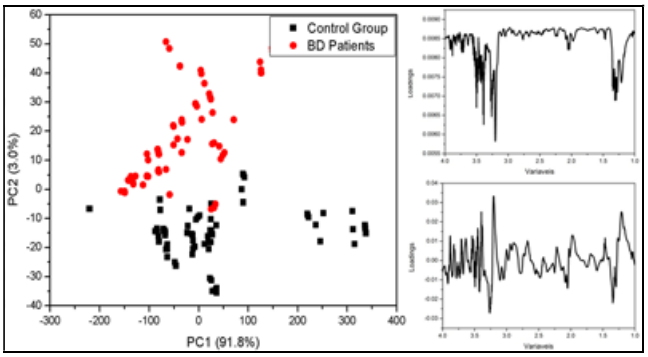

Figure 2: PCA results showing loading graphs for PC1 (upper panel) and PC2 (lower panel); total of 46 samples (21 BD and 25 HC) accounting for 138 spectra (63 BD and 75 HC) using region of δ 1.00 a 4.00 were used. 2 outliers were excluded from the analysis (one from each group).

Conclusions

From the presented results, it can be concluded that metabolites with signals in ¹H NMR spectral region from 1.00 to 4.00 ppm are crucial for the separation of groups studied, pointing for the potential key-metabolites as biomarkers for BD. To date, 18 compounds have been listed as possible key-metabolites, being principally amino acids and lipids.

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